



49321-16.ST25.txt
SEQUENCE LISTING

RECEIVED
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TECH CENTER 1600/2900

<110> Clinton, Gail M.
Evans, Adam
Henner, William D.

<120> HER-2 BINDING ANTAGONISTS

<130> 49321-16

<140> US 09/506,079
<141> 2000-02-16

<150> US 09/234,208
<151> 1999-01-20

<160> 13

<170> PatentIn version 3.2

<210> 1
<211> 79
<212> PRT
<213> Homo sapiens

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<222> (2)..(2)
<223> Applicants herein disclose Thr and Ser sequence variants at this position

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<222> (5)..(5)
<223> Applicants herein disclose Leu and Pro sequence variants at this position

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<223> Applicants herein disclose Pro and Leu sequence variants at this position

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<223> Applicants herein disclose Leu and Gln sequence variants at this position

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<223> Applicants herein disclose Met and Leu sequence variants at this position

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<222> (21)..(21)

<223> Applicants herein disclose Gly, Asp, Ala and Val sequence variants at this position

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<222> (36)..(36)

<223> Applicants herein disclose Leu and Ile sequence variants at this position

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<222> (54)..(54)

<223> Applicants herein disclose Pro and Arg sequence variants at this position

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<222> (64)..(64)

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<222> (73)..(73)

<223> Applicants herein disclose Asp and Asn sequence variants at this position

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Gly Xaa His Ser Xaa Xaa Pro Arg Pro Ala Ala Val Pro Val Pro Xaa
1 5 10 15

Arg Xaa Gln Pro Xaa Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
20 25 30

Ser Trp Asp Xaa Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
35 40 45

Ser Pro Thr Ser Val Xaa Ile Ser Pro Val Ser Val Gly Arg Gly Xaa
50 55 60

Asp Pro Asp Ala His Val Ala Val Xaa Leu Ser Arg Tyr Glu Gly
65 70 75

<210> 2

<211> 419

<212> PRT

<213> Homo sapiens

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<222> (342)..(342)

<223> Applicants herein disclose Thr and Ser sequence variants at this

position

<220>
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<222> (345)..(345)
<223> Applicants herein disclose Leu and Pro sequence variants at this position

GFD
Conf
<220>
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<223> Applicants herein disclose Pro and Leu sequence variants at this position

<220>
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<222> (356)..(356)
<223> Applicants herein disclose Leu and Gln sequence variants at this position

<220>
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<222> (358)..(358)
<223> Applicants herein disclose Met and Leu sequence variants at this position

<220>
<221> MISC_FEATURE
<222> (361)..(361)
<223> Applicants herein disclose Gly, Asp, Ala and Val sequence variants at this position

<220>
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<222> (376)..(376)
<223> Applicants herein disclose Leu and Ile sequence variants at this position

<220>
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<223> Applicants herein disclose Pro and Arg sequence variants at this position

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<222> (404)..(404)
<223> Applicants herein disclose Pro and Leu sequence variants at this position

<220>
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<223> Applicants herein disclose Asp and Asn sequence variants at this position

<400> 2

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu

1 5 10 15
 Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
 20 25 30
 Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
 35 40 45
 Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60
 Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80
 Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
 85 90 95
 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
 100 105 110
 Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
 115 120 125
 Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
 130 135 140
 Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
 145 150 155 160
 Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
 165 170 175
 Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
 180 185 190
 His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
 195 200 205
 Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
 210 215 220
 Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
 225 230 235 240

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Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275 280 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290 295 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305 310 315 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325 330 335

Pro Cys Ala Arg Gly Xaa His Ser Xaa Xaa Pro Arg Pro Ala Ala Val
340 345 350

Pro Val Pro Xaa Arg Xaa Gln Pro Xaa Pro Ala His Pro Val Leu Ser
355 360 365

Phe Leu Arg Pro Ser Trp Asp Xaa Val Ser Ala Phe Tyr Ser Leu Pro
370 375 380

Leu Ala Pro Leu Asp Pro Thr Ser Val Xaa Ile Ser Pro Val Ser Val
385 390 395 400

Gly Arg Gly Xaa Asp Pro Asp Ala His Val Ala Val Xaa Leu Ser Arg
405 410 415

Tyr Glu Gly

<210> 3
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> HER-2-specific oligonucleotide primer

<400> 3
tgagcaccat ggagctggc

<210> 4
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> HER-2-specific oligonucleotide primer

<400> 4
 tccggcagaa atgccaggct cc 22

<210> 5
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> HER-2 cDNA-specific oligonucleotide primer

<400> 5
 aacacagcgg tgtgagaagt gc 22

<210> 6
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 <212> DNA
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 <223> HER-2 ECDIIIa-region-specific oligonucleotide primer

<400> 6
 ataccgggac aggtcaacag c 21

<210> 7
 <211> 20
 <212> DNA
 <213> Artificial Sequence

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<400> 7
 tctgggtacc cactcactgc 20

<210> 8
 <211> 22
 <212> DNA
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<220>
 <223> HER-2 exon-specific oligonucleotide primer

<400> 8
 ttcacactgg cacgtccaga cc 22

<210> 9
 <211> 27
 <212> DNA
 <213> Artificial Sequence

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 <223> HER-2 cDNA-specific oligonucleotide primer

<400> 9
 gcacggatcc atagcagact gaggagg

27

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 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (1)..(240)
 <223> ECDIIIa region coding sequence

<220>
 <221> misc_feature
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 <223> Applicants disclose C, T, A and G variants at this position

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 Gly Xaa His Ser Xaa Xaa Pro Arg Pro Ala Ala Val Pro Val Pro Xaa
 1 5 10 15

cgc atr cag cct gnc cca gcc cac cct gtc cta tcc ttc ctc aga ccc 96
 Arg Xaa Gln Pro Xaa Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
 20 25 30

tct tgg gac mta gtc tct gcc ttc tac tct cta ccc ctg gcc ccc ctc 144
 Ser Trp Asp Xaa Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
 35 40 45

agc cct aca agt gtc cst ata tcc cct gtc agt gtg ggg agg ggc cyg 192
 Ser Pro Thr Ser Val Xaa Ile Ser Pro Val Ser Val Gly Arg Gly Xaa
 50 55 60

gac cct gat gct cat gtg gct gtt sac ctg tcc cgg tat gaa ggc tga 240
 Asp Pro Asp Ala His Val Ala Val Xaa Leu Ser Arg Tyr Glu Gly
 65 70 75

<210> 11
 <211> 79
 <212> PRT
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<400> 11

49321-16.ST25.txt

Gly Thr His Ser Leu Leu Pro Arg Pro Ala Ala Val Pro Val Pro Leu
 1 5 10 15

Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
 20 25 30

Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
 35 40 45

Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
 50 55 60

Asp Pro Asp Ala His Val Ala Val Asn Leu Ser Arg Tyr Glu Gly
 65 70 75

<210> 12
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 <212> PRT
 <213> Homo sapiens

<400> 12

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1 5 10 15

Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
 20 25 30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
 35 40 45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
 85 90 95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
 100 105 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
 115 120 125

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Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
 130 135 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
 145 150 155 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
 165 170 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
 180 185 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
 195 200 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
 210 215 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
 225 230 235 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
 245 250 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
 260 265 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
 275 280 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
 290 295 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
 305 310 315 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
 325 330 335

Pro Cys Ala Arg Gly Thr His Ser Leu Leu Pro Arg Pro Ala Ala Val
 340 345 350

Pro Val Pro Leu Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
 355 360 365

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Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
370 375 380

Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385 390 395 400

Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asn Leu Ser Arg
405 410 415

Tyr Glu Gly

<210> 13
<211> 1255
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<300>
<301> Coussens,L., Yang-Feng,T.L., Liao,Y.-C., Chen,E., Gray,A.,
<302> Tyrosine kinase receptor with extensive homology to EGF receptor
<303> Science
<304> 230
<305> 4730
<306> 1132-1139
<307> 1985-06-12

<400> 13

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1 5 10 15

Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
 115 120 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
 130 135 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
 145 150 155 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
 165 170 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
 180 185 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
 195 200 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
 210 215 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
 225 230 235 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
 245 250 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
 260 265 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
 275 280 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
 290 295 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
 305 310 315 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
 325 330 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu

340

345

350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
 355 360 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
 370 375 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
 385 390 395 400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
 405 410 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
 420 425 430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
 435 440 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
 450 455 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
 465 470 475 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
 485 490 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
 500 505 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
 515 520 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
 530 535 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
 545 550 555 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
 565 570 575

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Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
 580 585 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
 595 600 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
 610 615 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
 625 630 635 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Val Ser
 645 650 655

Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
 660 665 670

Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
 675 680 685

Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
 690 695 700

Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
 705 710 715 720

Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
 725 730 735

Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
 740 745 750

Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
 755 760 765

Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
 770 775 780

Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
 785 790 795 800

Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
 805 810 815

49321-16.ST25.txt

Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
820 825 830

Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
835 840 845

Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
850 855 860

Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
865 870 875 880

Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
885 890 895

Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
900 905 910

Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
915 920 925

Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
930 935 940

Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
945 950 955 960

Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
965 970 975

Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
980 985 990

Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
995 1000 1005

Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr
1010 1015 1020

Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly
1025 1030 1035

Ala Gly Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg
1040 1045 1050

Ser Gly Gly Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu
1055 1060 1065

Glu Ala Pro Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser
1070 1075 1080

Asp Val Phe Asp Gly Asp Leu Gly Met Gly Ala Ala Lys Gly Leu
1085 1090 1095

Gln Ser Leu Pro Thr His Asp Pro Ser Pro Leu Gln Arg Tyr Ser
1100 1105 1110

Glu Asp Pro Thr Val Pro Leu Pro Ser Glu Thr Asp Gly Tyr Val
1115 1120 1125

Ala Pro Leu Thr Cys Ser Pro Gln Pro Glu Tyr Val Asn Gln Pro
1130 1135 1140

Asp Val Arg Pro Gln Pro Pro Ser Pro Arg Glu Gly Pro Leu Pro
1145 1150 1155

Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu Arg Ala Lys Thr Leu
1160 1165 1170

Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val Phe Ala Phe Gly
1175 1180 1185

Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln Gly Gly Ala
1190 1195 1200

Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala Phe Asp
1205 1210 1215

Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala Pro
1220 1225 1230

Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr
1235 1240 1245

Leu Gly Leu Asp Val Pro Val
1250 1255